IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants:	Bruce A. Yankner and Philip Nadeau		
Serial No.:	10/086,398	Art Unit:	1617
Filed:	February 28, 2002	Examiner:	Theodore J. Criares
For:	*METHODS FOR DECREASING BETA AMYLOID PROTEIN*		

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF TO EXAMINER'S ANSWER

Sir:

This is a reply to the Examiner's Answer mailed on February 9, 2005 in the above-identified patent application. A request for Oral Hearing is enclosed along with the appropriate fee for a large entity. It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Appellants have appealed the rejection of claims 23-29 in the Office Action mailed February 24, 2004. A Notice of Appeal was filed on July 23, 2004. An Appeal Brief was filed September 23, 2004.

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(8) FURTHER ARGUMENT

(a) Rejections Under 35 U.S.C. § 102

Claims 23-29 were rejected under 35 U.S.C. § 102 (b) as anticipated by U.S. Patent No. 4,866,090 to Hoffman *et al.*. ("Hoffman"); U.S. Patent No. 5,350.758 to Wannamaker *et al.* ("Wannamaker"); and U.S. Patent No. 5,362,732 to Spielvogel *et al.* ("Spielvogel"). The crux of the Examiner's rejection is that the prior art inherently discloses compositions decreasing the production of Aβ by decreasing blood cholesterol levels because the prior art discloses the same compounds claimed by the applicants and these compounds are well-known anti-cholesterol agents.

The Legal Standard

Inherent anticipation requires that the missing descriptive material is 'necessarily present,' not merely probably or possibly present, in the prior art. *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citing *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991)). The mere fact that a certain thing *may result* from a given set of circumstances is insufficient to prove anticipation. *Electro Medical Systems, S.A. v. Cooper Life Sciences, Inc.* 34 F.3d 1048, 32 USPQ2d 1017 (Fed. Cir. 1994).

The Prior Art

Hoffman discloses analogs of lovastatin and related analogs which are useful alone or in combination with bile acid sequestrants as antihypercholesterolemic agents "for the treatment of arteriosclerosis, hyperlipidemia, familial hypercholesterolemia and like diseases in humans".

Wannamaker discloses pharmaceutical compositions which are inhibitors of cholesterol biosynthesis and are useful in lowering serum cholesterol levels in patients having chronically and significantly elevated cholesterol levels, particularly for treatment of atherosclerosis (background of the invention).

Spielvogel discloses a class of boronated compounds that have many different properties (anti-cancer, anti-inflammatory, analgesic, antiinfective) and which might also include activity in lowering cholesterol. This is a hypothetical disclosure that provides such a broad range that it encompasses everything and enables nothing.

The Claimed Invention

The claims on appeal define a composition comprising (1) ***an effective amount*** of (2) a compound decreasing blood cholesterol levels (3) **to decrease Aβ production by neuronal cells in an individual at risk of developing Alzheimers**. To anticipate, the prior art must disclose each of the claimed elements.

The prior art does discose a compound decreasing blood cholesterol levels.

However, the prior art fails to teach the other two claimed elements. There is no teaching or suggestion in the prior art that the compounds disclosed have any effect on the production of Aβ protein in neuronal cells.

The prior art fails to define what an effective dosage would be to achieve this endpoint. The dosages that are effective in lowering the amount of amyloid precursor protein to decrease production of Aβ are different when compared to those for lowering cholesterol to treat or prevent atherosclerosis. The appellants disclose that a 10% decrease in serum cholesterol levels is believed to be sufficient to decrease production of Aβ protein in neurons (page 3, lines 11-13). Such a decrease is not described in the prior art as being clinically effective in treating hypercholesterolemia (see, for example, Spielvogel, Example 15).

(b) Rejections Under 35 U.S.C. § 103

Claims 26-27 are rejected under 35 U.S.C. 103 (a) as being unpatentable over U.S. Patent No. 5,350,758 to Wannamaker *et al.* ("Wannamaker").

The Legal Standard

The U.S. Patent and Trademark Office has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. *In re Warner et al.*, 379 F.2d 1011, 154 U.S.P.Q. 173, 177 (C.C.P.A. 1967), *In re Fine,* 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988). In rejecting a claim under 35 U.S.C. § 103, the Examiner must establish a *prima facie* case that: (i) the prior art suggests the claimed invention; and (ii) the prior art indicates that the invention would have a reasonable likelihood of success. *In re Dow Chemical Company,* 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988).

The prior art must provide one of ordinary skill in the art with the motivation to make the proposed modifications needed to arrive at the claimed invention. *In re Geiger*, 815 F.2d 686, 2 U.S.P.Q.2d 1276 (Fed. Cir. 1987); *In re Lalu and Foulletier*, 747 F.2d 703, 705, 223 U.S.P.Q.

1257, 1258 (Fed. Cir. 1984). Claims for an invention are not *prima facie* obvious if the primary references do not suggest all elements of the claimed invention and the prior art does not suggest the modifications that would bring the primary references into conformity with the application claims. *In re Fritch*, 23 U.S.P.Q.2d, 1780 (Fed. Cir. 1992). *In re Laskowski*, 871 F.2d 115 (Fed. Cir. 1989). The Court of Appeals for the Federal Circuit warned that "the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for showing of the teaching or motivation to combine prior art references." *In re Dembiczak* , 175 F.3d 994 at 999 (Fed. Cir. 1999). The "question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination. *WMS Gaming, Inc. v International Game Technology*, 184 F.3d 1339 at 1355 (Fed. Cir. 1999). "[T]he showing must be clear and particular." *In re Dembiczak*, 175 F.3d 994 at 999 (Fed. Cir. 1999). Although with the answer in hand, the "solution" now appears obvious, that is not the test. The references must themselves lead those in the art to what is claimed.

The references here do not disclose the disorder to be treated, the selection of the composition to be used, nor the amount of active agent required. The composition therefore cannot be obvious.

The Prior Art

Claims 26 and 27 were rejected as obvious under 35 U.S.C. 103(a) as obvious over U.S. Patent No. 5,350,758 to Wannamaker *et al.* ("Wannamaker").

Claims 26 and 27 are dependent on claim 23 and are directed to compounds which inhibit uptake of dietary cholesterol and which block or decrease endogenous cholesterol production, respectively. Claim 23 defines a composition for decreasing the production of Aβ comprising an effective amount of a compound decreasing blood cholesterol levels to decrease Aβ production by neuronal cells in an individual at risk of developing Alzheimers. Wannamaker describes pharmaceutical compositions which are useful as inhibitors of squalene epoxidase and/or oxidosqualene cyclase and as a result inhibit cholesterol biosynthesis (col. 1, lines 10-13).

There is no teaching or suggestion that the compounds disclosed would have any effect on the production of Aβ in neuronal cells. Accordingly, one of ordinary skill in the art would not be motivated to make or use, nor enabled to make or use, the compounds disclosed by Wannamaker in an effective amount to inhibit the production of Aβ protein in neuronal cells.

(4) SUMMARY AND CONCLUSION

The prior art discloses a composition comprising cholesterol lowering in a dosage formulation for administration to an individual in need of cholesterol reduction. The prior art does not suggest that compounds lowering cholesterol would have any effect on Aβ production in neuronal cells. The dosages required to decrease production of Aβ protein are different from those required to treat atherosclerosis, and presumably the mechanism involved is quite different, since one there is no correlation between cholesterol and Aβ plaques. Since the dosage is different, the claims to the composition define a novel and non-obvious composition, if not a novel compound.

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The prior art does not disclose the use of cholesterol lowering agents to decrease production of Aβ protein and therefore does not lead one to the selection of a compound lowering cholesterol and the testing of the compound to determine a dosage required for one of ordinary skill in the art to use the compound to lower Aβ levels.

For the foregoing reasons, claims 23-29 are patentable.

Respectfully submitted,

Patrea L. Pabst
Reg. No. 31,284

Date: April 11, 2005

PABST PATENT GROUP LLP
400 Colony Square, Suite 1200
1201 Peachtree Street
Atlanta, Georgia 30361
(404) 879-2151
(404) 879-2160 (Facsimile)